

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 August 2003 (28.08.2003)

PCT

(10) International Publication Number
WO 03/070283 A3

- (51) International Patent Classification⁷: **C12N 15/11, A61K 48/00**
- (21) International Application Number: **PCT/EP03/01809**
- (22) International Filing Date: 21 February 2003 (21.02.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
02003982.2 22 February 2002 (22.02.2002) EP
02011074.8 17 May 2002 (17.05.2002) EP
02025103.9 8 November 2002 (08.11.2002) EP
- (71) Applicant and
(72) Inventor: **STREBHARDT, Klaus** [DE/DE];
Biedenkopfer Weg 24, 60489 Frankfurt (DE).
- (72) Inventors; and
(75) Inventors/Applicants (for US only): **SPÄNKUCH-SCHMITT, Birgit** [DE/DE]; Humboldtstrasse 72, 60318 Frankfurt (DE). **YUAN, Juping** [CN/DE]; Moulins-Ring 7, 61118 Bad Vilbel (DE).
- (74) Agents: **WEICKMANN, Franz, Albert et al.**; Weickmann & Weickmann, Postfach 860 820, 81635 München (DE).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Declaration under Rule 4.17:**
— of inventorship (Rule 4.17(iv)) for US only
- Published:**
— with international search report
- (88) Date of publication of the international search report:
24 December 2003
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: AGENT FOR INHIBITING DEVELOPMENT OR PROGRESS OF PROLIFERATIVE DISEASES AND ESPECIALLY CANCER DISEASES AND PHARMACEUTICAL COMPOSITION CONTAINING SAID AGENT

(57) Abstract: The present invention concerns inhibition of the activity of PLK1, which seems to be connected with cancer growth. Duplex RNAs antisense oligonucleotides and inhibitory peptides have been found to be useful in such inhibition, therefor they are claimed as ingredients for pharmaceutical compositions for the treatment of proliferative diseases, preferably cancer of various types.

WO 03/070283 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/01809

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/11 A61K48/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| X | WOLF G. ET AL.,: "inhibition of tumor cell proliferation in vitro by antisense oligonucleotides directed against the serine-threonine-kinase PLK" PATHOLOGY RESEARCH AND PRACTICE, vol. 196, no. 6, 7 June 2000 (2000-06-07), page 352 XP009015275 the whole document | 1-31 |
| X | WOLF G. ET AL.,: "antitumor activity of an antisense oligodeoxynucleotide targeted against human polo-like kinase PLK" INT. J. OF MOLECULAR MEDICINE, vol. 6, no. supp, - 2000 page s80 XP009015274 the whole document | 1-31 |
| | --- -/-- | |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

25 August 2003

Date of mailing of the international search report

08/09/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax (+31-70) 340-3018

Authorized officer

Mueller, F

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/01809

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| Y | YUAN J. ET AL.,: "polo-like kinase, a novel marker for cellular proliferation" AM. J. PATHOL., vol. 150, no. 4, April 1997 (1997-04), pages 1165-1172, XP009015248 see whole ----- | 1-31 |
| Y | US 6 183 961 B1 (BERNSTEIN HAROLD S ET AL) 6 February 2001 (2001-02-06) see whole doc. esp. col.9,2.par. ----- | 1-31 |
| A | THOMPSON J D: "Applications of antisense and siRNAs during preclinical drug development" DRUG DISCOVERY TODAY, ELSEVIER SCIENCE LTD, GB, vol. 7, no. 17, 1 September 2002 (2002-09-01), pages 912-917, XP002236964 ISSN: 1359-6446 the whole document ----- | |
| A | TUSCHL T: "RNA interference and small interfering RNAs" CHEMBIOCHEM - A EUROPEAN JOURNAL OF CHEMICAL BIOLOGY, WILEY VCH, WEINHEIM, DE, vol. 2, no. 4, April 2001 (2001-04), pages 239-245, XP002961590 ISSN: 1439-4227 the whole document ----- | |
| P,X | SPAENKUCH-SCHMITT B. ET AL.,: "inhibition of polo-like kinase 1 by antisense oligonucleotides and RNA interference" EUROPEAN J. OF CANCER, vol. 38, no. supp7, - 22 November 2002 (2002-11-22) page s144 XP002250181 the whole document ----- | 1-31 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/01809

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 31 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/01809

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|---|----|---------------------|----------------------------|---------------------|
| US 6183961 | B1 | 06-02-2001 | US 2002127702 A1 | 12-09-2002 |